REMARKS

Claims 1-3 and 6-13 are pending in the present application and under examination. Claims 1-3 and 6-8 were previously withdrawn. In the Office Action mailed on March 1, 2010, all of the pending claims were rejected.

I. Rejections Under 35 USC § 103(a) – Wang *et al.*

Claims 9-11 and 13 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Wang *et al.* (W0200277183) in view of Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pgs 53-137, 1989).

Claim 12 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable (1) over Wang *et al.* (WO2002077183, October 3 2002) and Harlow and Lane (Antibodies a Laboratory Manual) as applied to claims 9-11 and 13 above and further in view of Telford *et al.* (WO 02/34771 May 2, 2002).

Applicants respectfully maintain their traversal of the rejection and its supporting remarks. The Office has failed to establish a *prima facie* case of obviousness.

A. Motivation to Select the Cited Polypeptide

The Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007), made clear that there must be a clearly articulated reason why the claimed invention would have been obvious to support any rejection under 35 U.S.C. § 103 (see also MPEP § 2141 (III)). The Examiner has not provided any reason why one of skill in the art would want to make antibodies to the specific polypeptide encoded by "essential gene #23372" rather than antibodies to any of the other over 36,000 gene products disclosed in Wang *et al.* Since Wang *et al.* do not disclose antibodies to the polypeptide encoded by "essential gene #23372" specifically, Wang *et al.* at best discloses a broad genus of antibodies. In assessing obviousness of a genus as indicated in MPEP 2144.08, the Examiner "should determine whether it would have been obvious to one of

ordinary skill in the relevant art to make the claimed invention as a whole, *i.e.*, ***to select the claimed species or subgenus from the disclosed prior art genus***." The Examiner has made no such finding. Therefore the claims are not obvious in light of Wang *et al.* unless the Examiner can establish that one of skill in the art would want to make antibodies to the polypeptide encoded by "essential gene #23372" out of the over 36,000 disclosed gene products.

B. For a Composition to be Obvious under 35 U.S.C. 103(a) it must have a Utility

The Office states that Applicants repeatedly argue the incorrect statute over the combinations of Wang *et al.*, and asserts that "the rejections have been made under 35 USC 103 and not 35 USC 101."

Applicants respectfully disagree that they have been arguing the incorrect statute. Applicants are ***not*** arguing under the 35 U.S.C. 101 statute to rebut the rejection. The MPEP indicates that it cannot be obvious under 35 U.S.C. 103(a) to make a composition that has no ***utility*** (See, e.g., MPEP § 2144.09).

> If the prior art does not teach any ***specific or significant utility*** for the disclosed compounds, then the prior art is ***unlikely to render structurally similar claims prima facie obvious*** in the absence of any reason for one of ordinary skill in the art to make the reference compounds or any structurally related compounds. *In re Stemniski*, 444 F.2d 581, 170 USPQ 343 (CCPA 1971). (emphasis added)

The rationale is quite simple, if a composition has no real-world utility, why would one of skill in the art make such a composition. Unfortunately, the MPEP in the sections on 35 U.S.C. 103(a) does not provide guidance about what is a sufficient utility that would give one of skill in the art a reason to make a composition to support an obviousness rejection. Therefore, the Applicants referred to the utility standard under 35 U.S.C. 101 by way of analogy as the utility standard under 35 U.S.C. 101 is quite low. Given how low a standard it is, it is therefore reasonable to use in determine whether it is obvious to make the claimed composition.

It was in this context that Applicants pointed to the utility guidelines for patentable inventions provided in MPEP§ 2107.01 (I) (B), which describes that "substantial utility" (i.e.,

specific or significant utility) defines a "real world" use for a given invention. As noted in the previous response, MPEP § 2107.01 (I)(B) states:

> the following are examples of ***situations that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use*** and, therefore, do not define "substantial utilities":
>
> (A)Basic research such as studying the properties of the claimed product itself or the mechanisms in which the material is involved;
>
> (B)A method of treating an unspecified disease or condition;
>
> (C)A method of assaying for or identifying a material that itself has no specific and/or substantial utility;
>
> (D)A method of making a material that itself has no specific, substantial, and credible utility; and
>
> (E)A claim to an intermediate product for use in making a final product that has no specific, substantial and credible utility.
>
> (emphasis added)

Based on MPEP § 2144.09 (VI) and the guidelines provided in MPEP§ 2107.01 (I)(B), Applicants respectfully assert that Wang *et al.* does not provide a "specific or significant utility." While the Office states that Wang *et al.* disclose a polypeptide (encoded by "essential gene #23372") that is 99.2% identical as compared with SEQ ID NO: 207, the Examiner has not demonstrated that Wang *et al.* provide a "real world" use for the disclosed polypeptide. In the Office Action dated August 28, 2009, the Examiner cited to three rather long paragraphs in support of Wang *et al.* teaching antibodies to the over 36,000 genes taught in Wang *et al.* The first paragraph merely states that monoclonal and polyclonal antibodies can be generated. However, the first paragraph cites to no utility for such antibodies at all. Similarly, the second paragraph cited by the Examiner merely indicates how antibodies might be generated, but still cite to no reason for generating antibodies to any of the over 36,000 genes much less to "essential gene #23372". Finally, the third paragraph cited by the Examiner is merely a protocol to how to generate antibodies without any asserted reason for actually making the antibodies. If Wang *et al.* provides no reason to make antibodies, Wang *et al.* provides no reason to make a composition comprising a polypeptide with an adjuvant to make such an antibody. Therefore, as indicated in MPEP § 2144.09, it would not be obvious in light of Wang *et al.* to make the claimed composition.

C. Secondary considerations – Surprising Results

Even if the Examiner had established a *prima facie* case of obviousness, the Applicants have demonstrated that the claimed composition will produce an unexpected result. At the time the present application was filed, the polypeptide NMB1799 was not recognized to be a membrane protein. It was annotated as a metabolic protein "S-adenosylmethionine synthetase." One of skill in the art would expect that a protein involved in the metabolism would be expressed in the cytoplasm, not on the cell surface. *See, e.g.*, page 40, lines 32-34 of the specification. Proteins that are not on the surface of a bacterial cell cannot be used to immunize a subject against the bacteria. Any antibodies generated by such a protein will not recognize and bind to the bacteria since the protein is only found inside the cell. For a protein to be useful, it has to be on the surface of the bacteria where the immune system can access it.

The inventors discovered that NMB1799 is unexpectedly located in the membrane of *Neisseria meningitidis*. Thus, the inventors have shown that the protein can be used in an immunogenic composition and is a target for vaccine development. This is an important finding as most proteins in bacteria are not accessible to circulating antibodies in a host organism. Wang *et al.* does not teach or suggest that NMB1799 is surface exposed. Based upon this unexpected finding, the claimed composition therefore has a surprising utility in that it can be used to generate an immune response against *N. meningitidis* bacteria. This is shown on page 40, lines 25-34, of the specification. Humans immunized with outer membrane vesicles from two different strains of *N. meningitidis* produced antibodies against NMB1799. This proves that NMB1799 is surface exposed and capable of generating an immune response against *N. meningitis* bacteria.

This unexpected utility is sufficient to rebut any *prima facie* case of obviousness.

D. Conclusion

For at least the reasons set forth above, the Examiner has failed to make a *prima facie* case of obviousness for claims 9-13. Even if the Examiner has established a *prima facie* case of obviousness, the Applicants have obtained an unexpected result using the claimed composition. Applicants thus respectfully request that this basis for rejection be withdrawn.

II. Rejections Under 35 USC § 103(a) – Tettelin *et al.*

Claims 9-11 and 13 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tettelin *et al.* (Science, 287: 1809-1815, 2000; of record on 1449) in view of Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pgs 53-137, 1989) and Campbell (Monoclonal Antibody Technology, Chapter 1 pages 1-32, Elsevier Science Publishing Company, Inc., 1986, section 1.3.4).

Claim 12 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable (1) over Wang *et al.* (WO2002077183, October 3 2002) and Harlow and Lane (Antibodies a Laboratory Manual) as applied to claims 9-11 and 13 above and further in view of Telford *et al.* (WO 02/34771 May 2, 2002) and (2) over Tettelin *et al.* (Science, 287: 1809-1815, 2000), Harlow and Lane (Antibodies a Laboratory Manual, Cold Spring Harbor Laboratory, Chapter 5, pgs 53-137, 1989) and Campbell (Monoclonal Antibody Technology, Chapter 1 pages 1-32, Elsevier Science Publishing Company, Inc., 1986, section 1.3.4) as applied to claims 9-11 and 13 above and further in view of Telford *et al.* (WO 02/34771, May 2 2002).

Applicants respectfully maintain their traversal of the rejection and its supporting remarks. The Office has failed to establish a *prima facie* case of obviousness.

A. Motivation to Select the Cited Polypeptide

As discussed above, the Supreme Court in *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, 82 USPQ2d 1385 (2007), made clear that there must be a clearly articulated reason why the claimed invention would have been obvious to support any rejection under 35 U.S.C. § 103 (see also MPEP § 2141 (III)). The Examiner has not provided any reason why one of skill in the art would want to make antibodies to NMB1799 rather than antibodies to any of the other over 2,000 proteins disclosed in Tettelin *et al.* In assessing obviousness of a genus as indicated in MPEP 2144.08, the Examiner "should determine whether it would have been obvious to one of ordinary skill in the relevant art to make the claimed invention as a whole, *i.e.*, ***to select the claimed species or subgenus from the disclosed prior art genus***." The Examiner has made no such finding.

Therefore the claims are not obvious in light of Tettelin *et al.* unless the Examiner can establish that one of skill in the art would want to make antibodies to NMB1799 rather than to any of the other over 2,000 proteins disclosed by Tettelin *et al.*

B. For a Composition to be Obvious under 35 U.S.C. 103(a) it must have a Utility

As discussed above, the MPEP indicates that it cannot be obvious under 35 U.S.C. 103(a) to make a composition that has no ***utility*** (See, MPEP § 2144.09). The Examiner has asserted that that "bacterial proteins are used in the art to make antibodies for detection of infection by many different methodologies including western blotting." However, the Examiner's very statement proves that the asserted utility is not a utility that is specific to NMB1799. In fact, any of the over 2000 proteins disclosed in Tettelin *et al.* could have this asserted utility. Thus, the asserted utility is not a specific utility as required by MPEP § 2144.09 (VI) and 2107.01, which clearly indicate that prior art disclosures must have a "specific or significant utility" in order to render a claim obvious. In this case, even if it was obvious to combine the teachings of Tettelin *et al.* and Campbell to form an immunogenic composition for making antibodies against the NMB1799 polypeptide, the immunogenic composition of the theoretical combination of Tettelin *et al.* and Campbell cannot render the present claims obvious, because even if motivated to randomly select NMB1799 from among the over 2000 disclosed genes to generate antibodies, that composition would lack specific or significant utility, as the resulting antibodies would lack any specific or significant utility other than to use it to determine the utility of NMB1799 which falls under categories (A) and/or (C) of MPEP § 2107.01 (I)(B) of uses that are not sufficient to provide real world utility. For at least these reasons, the teachings of Tettelin *et al.* do not render obvious any of presently pending claims 9–13.

C. Secondary considerations – Surprising Results

Even if the Examiner had established a *prima facie* case of obviousness, the Applicants have demonstrated that the claimed composition will produce an unexpected result. At the time the present application was filed, the polypeptide NMB1799 was not recognized to be a membrane protein. It was annotated as a metabolic protein "S-adenosylmethionine synthetase." One of skill in the art would expect that a protein involved in the metabolism would be expressed in the cytoplasm,

not on the cell surface. *See, e.g.*, page 40, lines 32-34 of the specification. Proteins that are not on the surface of a bacterial cell cannot be used to immunize a subject against the bacteria. Any antibodies generated by such a protein will not recognize and bind to the bacteria since the protein is only found inside the cell. For a protein to be useful, it has to be on the surface of the bacteria where the immune system can access it.

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This unexpected utility is sufficient to rebut any *prima facie* case of obviousness.

D. Conclusion

For at least the reasons set forth above, the Examiner has failed to make a *prima facie* case of obviousness for claims 9-13. Even if the Examiner has established a *prima facie* case of obviousness, the Applicants have obtained an unexpected result using the claimed composition. Applicants thus respectfully request that this basis for rejection be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal form is separated from this document and the Patent and Trademark Office determines that an extension and/or other relief (such as payment of a fee under 37 C.F.R. § 1.17 (p)) is required, Applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of such petition and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing Docket No. **223002109500**.

Dated: September 1, 2010

Respectfully submitted,

By: /Otis Littlefield/
Otis B. Littlefield
Registration No.: 48,751

MORRISON & FOERSTER LLP
425 Market Street
San Francisco, California 94105-2482
Telephone: 415.268.6846
Fax: 415.268.7522